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EXAMINER	
BIANCHI, KRISTIN A	

ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
03/05/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/589,981	SHIMIZU ET AL.	
	Examiner	Art Unit	
	KRISTIN BIANCHI	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09/04/2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-116,122-129 and 136-144* is/are pending in the application.

4a) Of the above claim(s) *68-115,123-129 and 136-144* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-67,116 and 122* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-116, 122-129 and 136-144 are pending in the instant application. Claims 68-115, 123-129 and 136-144 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected subject matter. The withdrawn subject matter is patentably distinct from the elected subject matter as it differs in structure and element and would require separate search considerations. In addition, a reference which anticipates one group would not render obvious the other. Claims 1-67, 116 and 122 are rejected.

Election/Restrictions

As described in the interview summary filed on February 24, 2010, the compound which was searched and examined in the previous Office Action dated November 23, 2009 (compound r192) was not Applicant's intended elected compound (192). Therefore, the rejections presented in the previous Office Action have been withdrawn and replaced by those described below.

Applicant's election without traverse of Group I, claims 1-67, 116 and 122, and the compound 192 in the response filed on September 4, 2009 is acknowledged.

The examiner will follow the guidelines of MPEP 803.02 wherein once a species is elected, it is examined for compliance with all applicable statutes for patentability and if compliance is found, then the examination is expanded to a reasonable number of elated species to determine whether they also comply with the statute. The examiner will determine whether the entire scope of the claims is patentable according to MPEP 803.02.

Applicant's elected species appears allowable over the prior art of record. Therefore, according to MPEP 803.02: should no prior art be found that anticipated or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is found that anticipated or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The search of the Markush-type claim has been extended to the non-elected species wherein:

Z is -O- or -S-; D1-D4 are carbon; X is C; L is N; E, G, J, and M are C; R10 is hydrogen; R14 is (6) C1-6 alkyl group, (14) carbocyclic group, (15) heterocyclic group, or (16) bicyclic carbocyclic group or heterocyclic group; and the rest of the variables are as defined in claim 1.

As prior art has been found which anticipates the above identified nonelected species, the Markush-type claims are rejected as follows and the subject matter of the claims drawn to nonelected species held withdrawn from consideration. Claims 1-67, 116 and 122 have been examined to the extent that they are readable on the elected embodiment and the above identified nonelected species. Since art was found on the nonelected species, subject matter not embraced by the elected embodiment or the above identified nonelected species is therefore withdrawn from further consideration.

Priority

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d), a certified English translation of the foreign application (2004-045383) must be submitted in reply to this action. 37 CFR 41.154(b) and 41.202(e). Failure to provide

a certified translation may result in no benefit being accorded for the non-English application.

It is noted that Applicant's elected compound 192 is not disclosed in the foreign document.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 62, 66 and 67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, claims 62, 66 and 67 refer to compound numbers in the specification. Claims must, under modern claim practice, stand alone to define an invention, and incorporation into claims by express reference to the specification is not permitted. Ex parte Fressola, 27 USPQ 2d 1608 (1993).

This rejection can be overcome by amending the claims to include the structures of the compounds referenced.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-67, 116 and 122 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds of formula (I) or pharmaceutically acceptable salts thereof, does not reasonably provide enablement for

solvates thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

The state of the prior art/level of ordinary skill/level of predictability

Active pharmaceutical ingredients are frequently delivered to the patient in the solid-state as part of an approved dosage form (e.g., tablets, capsules, etc.). Solids provide a convenient, compact, and generally stable format to store an active pharmaceutical ingredient or a drug product. Understanding and controlling the solid-state chemistry of active pharmaceutical ingredients, both as pure drug substances and in formulated products, is therefore an important aspect of the drug development process. Active pharmaceutical ingredients can exist in a variety of distinct solid forms, including polymorphs, solvates, hydrates, salts, co-crystals, and amorphous solids. Each form displays unique physicochemical properties that can profoundly influence the bioavailability, manufacturability purification, stability, and other performance characteristics of the drug. Hence, it is critical to understand the relationship between the particular solid form of a compound and its functional properties.

For ionizable compounds, preparation of salt forms using pharmaceutically acceptable acids and bases is a common strategy to improve bioavailability. However, the preparation of other solid forms, such as polymorphs, solvates and hydrates, are not so common to be predictable. In order to obtain patent protection on these forms, some of which may have significantly different properties and relevance as development candidates, it is essential to prepare them, identify conditions for making them, and evaluate their properties as valuable new pharmaceutical materials.

Therefore, for the reasons above, the state of the prior art is one of unpredictability.

As stated above, crystalline solids can exist in the form of polymorph, solvates or hydrates. "Phase transitions such as polymorph interconversion, desolvation of solvate, formation of hydrate, and conversion of crystalline to amorphous form may occur during various pharmaceutical processes, which may alter the dissolution rate and transport characteristics of the drug. Hence, it is desirable to choose the most suitable and stable form of the drug in the initial stages of drug development" (Vippagunta et al., abstract). In further discussing the predictability of the formation of solvates, Vippagunta et al. discloses that "predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds" (page 18, section 3.4).

The amount of direction or guidance present/existence of working examples

A disclosure should contain representative examples which provide reasonable assurance to one skilled in the art that the compounds which fall within the scope of a claim will posses the alleged activity. The specification does not adequately enable a method of making the solvates of the compounds that the claims encompass.

There is no data present or any working examples in the specification for the preparation of solvates of said compounds.

Breadth of the claims

The instant breadth of the rejected claims is broader than the disclosure, specifically; the instant claims include any solvates of said compounds.

The quantity of experimentation needed

While the level of skill in the pharmaceutical arts is high, it would require undue experimentation for one of ordinary skill in the pertinent art to prepare any solvate of said compounds.

The specification provides limited support, as noted above, for the solvates encompassed by the claims. The quantity of experimentation needed to make the solvates encompassed by the claims would be an undue burden on one skilled in the chemical art, since the skilled artisan is given inadequate guidance for the reasons stated above. Also, the science of crystallization has evolved such that, without guidance or working examples in the specification, the claim lacks enablement.

This discussion established *prima facie* non-enablement. Deletion of the words "solvate" from the claims would overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 28, 29, 48, 49, 51-56, 58, 116, and 122 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 2004/018430. US Patent No. 7,560,558 is an equivalent document which is in written in English.

Specifically, US Patent No. 7,560,558 discloses compounds 261 (columns 399 and 400), 269 (columns 403 and 404), 274 (columns 405 and 406), and 431 (columns 471 and 472) which anticipate compounds of the instant claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

At least claim 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over at least claim 1 of U.S. Patent No. 7,560,558. Although the conflicting claims are not identical, they are not patentably distinct from each other from the reasons given below.

U.S. Patent No. 7,560,558 discloses compounds of formula (I) which are used for the same purpose as the compounds of the instant claims (i.e., they have TBFβ inhibitory activity). The compounds disclosed in U.S. Patent No. 7,560,558 are a subgenus of compounds which fall within the scope of the genus of the compounds of the instant claims.

MPEP § 2144.08.11.A.4(c) states "... consider teachings of a preferred species within the genus. If such a species is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties". This is the "Genus- Species Guidelines" for examination based on 35 USC 103 and an analogous guideline was followed here for the analysis of obviousness-type double patenting.

Therefore, it would have been obvious to one of ordinary skill in the art to make and use at least some of the compounds of the instant claims in view of U.S. Patent No. 7,560,558.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KRISTIN BIANCHI whose telephone number is (571)270-5232. The examiner can normally be reached on Mon-Fri 7am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kamal A Saeed/
Primary Examiner, Art Unit 1626

Kristin Bianchi
Examiner
Art Unit 1626

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